UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

EPA United States Environmental Protection Agency Office of Pesticide Programs

MEMORANDUM

10/10/2017

SUBJECT: Acute Toxicity Review for *Project Flash Spray*, EPA Reg. No.: **9480-RU**
DP 440586

FROM: Boris S. Yurchak, Chemist
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

THRU: Jenny Tao, Team Leader (Acute Toxicology)
Chemistry and Toxicology Team
Product Science Branch
Antimicrobials Division (7510P)

TO: Seiichi Murasaki/ Zebora Johnson
Regulatory Management Branch I
Antimicrobials Division (7510P)

Registrant: Professional Disposables International, Inc			
Action Code A540	Decision No.: 529432	Submission No.: 1003580	E-Sub No.: n/a
MRID No(s).: 50282503, 50282504, 50282505, 50282506, 50282507, 50282508			

Formulation from label			
PC code(s)	CAS #(s)	Active Ingredient(s)	% weight
000595	7722-84-1	Hydrogen Peroxide	4.04
		Other Ingredients	95.96
		Total	100.00

I. BACKGROUND

The Registrant, Professional Disposables International, Inc, has submitted six acute toxicity studies to support the application for pesticide registration of their product: *Project Flash Spray*, EPA Reg. No. 9480-RU. The proposed product is a disinfectant spray for hard non-porous non-food contact surfaces.

II. RELEVANT DOCUMENTS

	RECEIVED	N/A
EPA FORM 8570-1 – Application for Pesticide Registration	☒	☐
EPA FORM 8570-34 – Certification with respect to citation of data	☐	☒
EPA FORM 8570-35 – Data Matrix (7/11/2017)	☒	☐
Cover letter (5/9/2017)	☒	☐
Transmittal document	☒	☐
Proposed Basic CSF, (4/26/2017)	☒	☐
Proposed label, (4/26/2017)	☒	☐
	☐	☐
Acute Oral Toxicity Study (OSCPP 870.1100)	☒	☐
Acute Dermal Toxicity Study (OSCPP 870.1200)	☒	☐
Acute Inhalation Toxicity Study (OSCPP 870.1300)	☒	☐
Primary Eye Irritation Study (OSCPP 870.2400)	☒	☐
Primary Skin Irritation Study (OSCPP 870.2500)	☒	☐
Dermal Sensitization Study (OSCPP 870.2600)	☒	☐
Comment:		

III. FINDINGS/RECOMMENDATIONS

3.1. The submitted acute toxicity studies are all acceptable except for the Primary Skin Irritation study (MRID 50282507).

3.2. The Primary Skin Irritation study is deemed to be supplemental due to the unacceptable test result. Detailed comments are provided in the Data Review for this endpoint.

3.3. Each MRID is accompanied with an Affidavit confirming that the study was conducted on the proposed product *Project Flash Spray*.

3.4. The acute toxicity profile of *Project Flash Spray*, EPA Reg. No. 9480-RU, is currently:

GRN	Study	MRID	Toxicity Category	Status
870.1100	Acute Oral Toxicity	50282503	IV	Acceptable
870.1200	Acute Dermal Toxicity	50282504	IV	Acceptable
870.1300	Acute Inhalation Toxicity	50282505	IV	Acceptable
870.2400	Primary Eye Irritation	50282506	III	Acceptable
870.2500	Primary Skin Irritation	50282507	Undetermined	Supplemental
870.2600	Dermal Sensitization	50282508	Not a sensitizer	Acceptable

CONCLUSION:

The acute toxicity studies/data provided for the proposed product EPA Reg. No. 9480-RU have not yet satisfied the data requirements for its registration. Additional information is needed regarding the skin irritation study.

IV. PRODUCT LABELING

1. SIGNAL WORD: **CAUTION**

2. The statement, "**Keep Out of Reach of Children (KOROC)**", is required. It should appear immediately below the front-panel signal word "CAUTION".

3. The precautionary and first aid statements cannot be prescribed due to the data gap.

DATA REVIEW FOR ACUTE ORAL TOXICITY TESTING (OCSPP 870.1100)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282503

Reviewer: B. Yurchak
Study Completion Date: 3/9/2016
Project No.: 16-012-3

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid

Dose level: 5000 mg/kg

Animals: Rat, Sprague-Dawley albino strain
- **Sex:** 3 females
- **Age:** Young adults, 9-11 weeks old
- **Weight:** 229-232 g
- **Source:** Envigo, Indianapolis, Indiana

Method: Up-And-Down

Summary:
1. **Estimated LD_{50}:** > 5000 mg/kg
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviations from OPPTS 870.1100 and/or other comments: none

Results:

An initial limit dose of 5000 mg/kg was administered to one healthy female rat by oral gavage. Due to the absence of mortality in this animal, two additional females received the same dose level, simultaneously. Since these animals survived, no additional animals were tested. Females were selected for the test because they are frequently more sensitive to the toxicity of test compounds than males. All animals were observed for mortality, signs of gross toxicity, and behavioral changes at least once daily for 14 days after dosing. Body weights were recorded prior to administration (initial) and again on Days 7 and 14 (terminal) following dosing.

All animals survived test substance administration, gained body weight, and appeared active and healthy during the study. There were no signs of gross toxicity, adverse clinical effects, or abnormal behavior. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

Reported Mortality

Animal Number	Dose Level (mg/kg)	Short-Term Outcome	Long-Term Outcome
31	5000	O	O
32	5000	O	O
33	5000	O	O

O = Survival; X = Death

DATA REVIEW FOR ACUTE DERMAL TOXICITY TESTING (OCSPP 870.1200)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282504

Reviewer: B. Yurchak
Study Completion Date: 3/15/2016
Project No.: 16-012-4

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid

Dose level: 5000 mg/kg

Animals: New Zealand Albino rabbits
- **Sex:** 5 Males and 5 Females
- **Age:** Young adult 12 weeks
- **Weight:** 2.60-3.37 kg
- **Source:** Kuiper Rabbitry, Gary, Indiana

Summary:
1. **Estimated LD_{50}:** > 5000 mg/kg
2. **Toxicity Category:** IV
3. **Classification:** Acceptable

Deviation from Guideline 870.1200 and/or other comments: none

Results:

The undiluted test material was administered to five male and five female rabbits at a dose level of 5000 mg/kg.

Five thousand milligrams of the test substance per kilogram of body weight was applied evenly over a dose area of approximately 10% of the body surface and covered with two layers of porous gauze dressing and a sleeve of plastic sheeting was fitted over the shaved trunk of the animal and secured in place with non-irritating surgical tape. The rabbits were then returned to their designated cages. The day of application was considered Day 0 of the study.

After 24 hours of exposure to the test substance, the pads were removed and the test sites were gently cleansed with a 3% soap solution followed by tap water and a clean paper towel to remove any residual test substance.

All animals survived test substance administration, gained body weight, and appeared active and healthy during the study. All surviving animals exhibited edema and/or erythema at the application site. No gross abnormalities were noted for any of the animals when necropsied at the conclusion of the 14-day observation period.

Based on the lack of mortality observed, the acute dermal LD_{50} value was found to be greater than 5000 mg/kg.

Reported Mortality

Dose Level (mg/kg)	Number Dead / Number Tested		
	Males	Females	Combined
5000	0 / 5	0 / 5	0 / 10

DATA REVIEW FOR ACUTE INHALATION TOXICITY TESTING (OCSPP 870.1300)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282505

Reviewer: B. Yurchak
Study Completion Date: 3/11/2016
Project No.: 16-012-6

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid
Concentration: 2.28 mg/L (gravimetric)

Chamber Type: Nose-only chamber produced by Charles Spengler Associates of Cincinnati, Ohio

Animals: Rat, Sprague-Dawley albino strain

Sex:	5 Males and 5 Females
Age:	young adults, 8-12 weeks old
Weight:	215-246 grams
Source:	Envigo, Indianapolis, Indiana

Method: Limit Test (OCSPP 870.1300)

Summary:

1. **Estimated LC_{50}:** >2.28 mg/L
2. **Mean MMAD:** 2.6 µm; **Mean GSD:** 2.47
3. **Toxicity Category:** IV
4. **Classification:** Acceptable

Deviation from Guideline 870.1300 and/or other comments: none

Results:

After establishing the desired generation procedures during pre-test trials, ten healthy rats (5/sex) were exposed to the test atmosphere, nose only, for 4 hours. Chamber concentration and particle size distribution of the test substance were determined periodically during the exposure period. The animals were observed for signs of gross toxicity and behavioral changes at least once daily for 14 days. Bodyweights were recorded prior to exposure and again on days 7 and 14 (termination). Necropsies were performed on all animals at terminal sacrifice.

All animals survived exposure to the test atmosphere and gained bodyweight over the 14-day observation period. The gravimetric chamber concentration was 2. 28 mg/L. The mass median aerodynamic diameter was estimated to be 2.6 microns based on the particle size distribution as measured with an Anderson Cascade Impactor.

All animals were inactive, but otherwise appeared normal for the entire 14-day observation period. Gross necropsy findings at terminal sacrifice were generally unremarkable.

Reported Mortality

Exposure Concentration (mg/L)	Number dead / Number tested		
	Males	Females	Combined
2.28	0/5	0/5	0/10

Chamber Atmosphere

Exposure Conc. (mg/L)	MMAD (µm)	GSD
2.28	2.50	2.410
2.28	2.71	2.532
mean	2.60	2.47

Chamber Environment

Exposure Level (mg/L)	2.28
Nominal concentration (mg/L)	18.7
Chamber Volume (L)	400
Total Airflow Rate (Lpm)	87-94
Temperature (°C)	19.0-20.0
Relative Humidity (%)	40-50

DATA REVIEW FOR ACUTE EYE IRRITATION TESTING (OCSPP 870.2400)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282506

Reviewer: B. Yurchak
Study Completion Date: 1/18/2016
Project No.: 15-073-1

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid

Dosage: 0.1 mL

Animals: Rabbit, New Zealand albino
Number/Sex: 6 / male and/or female
Age: Young adult, 10-12 weeks
Weight: 2- 3 kg
Source: Kuiper Rabbitry, Gary, Indiana

Summary:

1. **Toxicity Category:** III
2. **Classification:** Acceptable

Deviations from Guideline 870.2400 and/or other comments: sex of animals is not identified

Results:

Six healthy animals were used for test purposes. Three animals were dosed in accordance with recommendations of OPPTS 870.2400: One-tenth of a milliliter of the test substance was then instilled into the conjunctival sac of the right eye of each rabbit by pulling the lower lid away from the eyeball. The upper and lower lids were then gently held together for about one second before releasing to minimize loss of the test substance. The other eye of each rabbit remained untreated with the test substance and served as a control.

Three additional animals were dosed and the eyes rinsed with approximately 35 mL of tap water following a 3-4 second contact period. *Since this method is not recommended, its result is not under following consideration.*

There was no corneal opacity observed in any treated eye during this study. 48 hours after test substance instillation, one treated eye exhibited "positive" conjunctivitis. The overall incidence

and severity of irritation decreased with time. All animals were free of ocular irritation by Day 3 (72 hrs). The test substance would be classified as Toxicity Category III.

Observations (No rinse)	Number "Positive" / Number Tested			
	Time After Instillation			
	1 hr	24 hrs	48 hrs	72 hrs
Corneal Opacity	0/3	0/3	0/3	0/3
Iritis	3/3	2/3	0/3	0/3
Conjunctivae				
Redness *	3/3	3/3	2/3	0/3
Chemosis *	3/3	2/3	0/3	0/3
Discharge**	3/3	3/3	0/3	0/3

* Score of 1 or more required to be considered "positive".

** Not considered a positive irritation effect; however, scores of 1 or greater are noted here for completeness.

DATA REVIEW FOR ACUTE DERMAL IRRITATION TESTING (OCSPP 870.2500)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282507

Reviewer: B. Yurchak
Study Completion Date: 3/4/2016
Project No.: 16-012-2

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid

Dosage: 0.5 mL

Animals: Rabbit, New Zealand albino
Sex: 3 Females
Age: Young adult, 10-12 weeks old
Weight: 2.82-3.39 kg
Source: Kuiper Rabbitry, Gary, Indiana

Summary:

1. **Toxicity Category:** Undetermined
2. **Classification:** Supplemental

PII: cannot be determined

Deviations from Guideline 870.2500 and/or other comments:

1. The first documented observation was conducted after 4.5 hours instead of recommended 1 hour. No justifications and/or explanations for such delay were provided in the study report. Under "Compound Administration" on page 9 of the study report, it was stated that "....., and 30 minutes after removal, the site was observed and scored." However, there is no documentation of dermal observation provided before 4.5 hours.
2. After 4 hours of exposure to the test substance, the excess material was removed from the site. As per the recommendation, residual test substance should be generally removed.

Results:

Five-tenths of a milliliter of the test substance was applied to one 6-cm^2 intact dose site on each animal. The test substance was then covered with a 2.5 cm^2 – 2 layer gauze patch held in place with non-irritating Kendal Curity Standard Porous Tape and the patch was then covered with a semi-occlusive plastic overwrap secured in place with Kendal Curity Standard Porous Tape for the duration of the exposure period.

At the end of the 4-hour contact period excess material was removed from the site; and 30 minutes after removal, the site was observed and scored.

Within 24 hours of patch removal, one treated site exhibited well-defined erythema and all three sites exhibited slight edema. The overall incidence and severity of irritation decreased gradually with time. All animals were free of erythema and edema by 72 hours. The Primary Irritation Index (PDII) was found to be 1.08 by the study laboratory based on erythema and edema making the test material a slight-irritant. The test material is classified in the study with EPA Toxicity Category IV.

Individual Dermal Irritation Scores following the four-hour exposure

ERYTHEMA/EDEMA

Animal No.	Sex	Time After Patch Removal				
		4.5 hrs	24 hrs	48 hrs	72 hrs	Day7
25	F	1/2	0/0	0/0	0/0	0/0
26	F	2/2	1/0	1/0	0/0	0/0
27	F	1/2	1/0	0/0	0/0	0/0
Avg		1.33/2.0	0.67/0	0.33/0	0/0	0/0
Total		3.33	0.67	0.33	0/0	0/0

$$PDII = \frac{3.33 + 0.67 + 0.33 + 0}{4} = 1.08$$

Note: The Primary Irritation Index (PDII) calculation is not acceptable because the Primary Skin Irritation score (3.33) for the first observation was calculated for 4.5 hours, instead of at 1 hour, after removal of the test substance.

DATA REVIEW FOR DERMAL SENSITIZATION TESTING (OPPTS 870.2600)

Product Manager: Seiichi Murasaki /33
MRID No.: 50282508

Reviewer: B. Yurchak
Study Completion Date: 4/11/2016
Project No.: 16-012-5

Testing Laboratory: Tox Monitor Laboratories, Inc
Author: Michael Kukulinski, B.S., L.A.T.G.

Quality Assurance (40 CFR §160): Included

Test Material: *Project Flash*, Clear liquid
Induction: 0.4 mL

Challenge: 0.4 mL

Animals: Guinea pig, Hartley albino strain

Test group: 20 Males

Naive control: 10 Males

Preliminary test: 2 Males

Age: young adult

Weight: 316 – 439 g

Source: Kuiper Rabbitry, Gary, Indiana

Historical Positive Control Study: 1-Chloro-2,4-dinitrobenzene

Guinea pig, Hartley albino; 20 animals (sex unknown)

Induction: 0.4 mL, 0.3% in 80% Ethanol

Challenge: 0.4 mL, 0.1% in Acetone

Conducted: 9/19/2015 (within 6 months of the current study)

Method: Buehler

Summary:

1. Not a sensitizer
2. **Classification:** Acceptable

Deviations from Guideline 870.2600 and/or other comments: none

Procedure Highlights:

- A 0.4 mL quantity of each test preparation was applied into a 25 mm Hill Top Chamber. The animal was placed into the restrainer and the chambers applied to the clipped surface as quickly as possible. The chambers were occluded with rubber dental dam pulled taut and fastened to the bottom of the restrainer with clips. The restrainer was adjusted to minimize movement of the animal during exposure.
- Exposure periods: 6 hours;
- Inductions: once/week for three weeks with the same dose (0.4 mL) at a 100% concentration; Challenge: 28 days after the first dose at a 75% concentration.

Results:

The study results are given in the tables below. All of the animals gained weight during the study.

The positive control study is provided in Appendix I of the MRID. The study evaluates the sensitivity of the test animals to the sensitization.

Ten guinea pigs served as a naïve control group, and remained untreated through the induction phase. Six naïve control animals received only the primary challenge dose, at a 75% concentration. The four remaining animals were designated for a re-challenge, if necessary. The incidence and severity of these responses in the test group were essentially comparable to those produced by the naïve control group indicating that sensitization had not been induced.

Response Indices - Erythema at Primary Challenge

Group	Incidence of Positive Response[1]		Severity[2]	
	24 Hrs	48 Hrs	24 Hrs	48 Hrs
Test Group	2 / 20	0 / 20	0.05	0.0
Naïve Control Group	1 / 6	0 / 6	0.08	0.0

[1] Number of erythema scores equal to 0.5 (slight, patchy erythema) per number of animals evaluated.

[2] Sum of the erythema scores divided by the number of animals evaluated.

Induction Scores of Project Flash
Lot #: PDI-0061-LO-938-135 2/17/2016

Test Group: (100% concentration)

	Induction 1		Induction 2		Induction 3	
Animal #	24 Hr	48Hr	24 Hr	48Hr	24 Hr	48Hr
67	0.5	0	0	0	0	0
68	1	0.5	0	0	0.5	0.5
69	0	0	0	0	0	0
70	0	0	0	0	0	0
71	0.5	0	0.5	0	0	0
72	1	0.5	0	0	1	0.5
73	1	0.5	1	0.5	0.5	0
74	0	0	0	0	0	0
75	0.5	0	0	0	0	0
76	0	0	0	0	0	0
77	0	0	0.5	0	0	0
78	0	0	0	0	0	0
79	1	0.5	0	0	0.5	0
80	0	0	0.5	0	0	0
81	0.5	0	0	0	1	1
82	0.5	0	0.5	0	1	0.5
83	1	0	0.5	0	0	0
84	0.5	0	0	0	0.5	0
85	0	0	0	0	0.5	0
86	0	0	0	0	0	0

SKIN GRADES FOLLOWING PRIMARY CHALLENGE:

Test Group: Project Flash
Lot #: PDI-0061-LO-938-135 2/17/2016 (75% Concentration)

Animal #	24 Hours	48 Hours
67	0	0
68	0	0
69	0	0
70	0	0
71	0	0
72	0	0
73	0	0
74	0	0
75	0	0
76	0.5	0
77	0	0
78	0	0
79	0	0
80	0	0
81	0	0
82	0	0
83	0	0
84	0.5	0
85	0	0
86	0	0
Mean	0.05	0

TABLE 3

SKIN GRADES FOLLOWING PRIMARY CHALLENGE:

Naive Control Group: Project Flash
Lot #: PDI-0061-LO-938-135 2/17/2016 (75% Concentration)

Animal #	24 Hours	48 Hours
87	0	0
88	0	0
89	0.5	0
90	0	0
91	0	0
92	0	0
Mean	0.08	0